

## **REMARKS/ARGUMENTS**

This Amendment is submitted in response to the Office Action mailed October 14, 2009. Claims 1 and 6 are currently pending in the application. Claims 7-11 were previously withdrawn. By this paper, new claims 12 and 13 are presented for the Examiner's consideration. Support for these new claims may be found in paragraph 31 of the specification as published.

## **REJECTION UNDER 35 U.S.C. §112 SECOND PARAGRAPH**

The Examiner rejected claims 1 and 6 under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. More specifically, the Office Action alleges that the definition in the specification does not provide a definitive scope for the term "pharmaceutical combination." Applicants respectfully traverse the rejection. Without prejudice, Applicants have amended claims 1 and 6 to speed prosecution of the application, as described below.

In the Office Action dated October 14, 2009, the Examiner contends that the definition of the term "pharmaceutical combination" uses open language and examples instead of providing a "definitive scope" to the term (pages 2-3). While reserving the right to pursue claims to the full scope of the term "pharmaceutical combination" in the future, Applicants have amended the claims to recite exemplary embodiments of a pharmaceutical combination as provided in the specification.

Specifically, claims 1 and 6 have been amended to recite a pharmaceutical composition comprising Gly<sub>2</sub>GLP-2 and exendin (9-39). Support for this amendment is found in the specification, such as at paragraph 31.

New claim 12 is drawn to another exemplary embodiment of a pharmaceutical combination found in the specification, where the inhibitor and the enhancer are formulated separately, but associated physically. Support for this new claim is also found in paragraph 31 of the specification as published. New dependent claim 13 is directed to one such contribution in the form of a kit.

Applicants respectfully submit that since the claims have been amended to recite plainly defined embodiments of a pharmaceutical combination, as found in the specification, the Examiner's rejection 35 U.S.C. §112, second paragraph should be withdrawn, and claims 1, 6, 12 and 13 are allowable.

### **REJECTION UNDER 35 U.S.C. §103**

The Examiner next rejected claims 1 and 6 as being obvious over Tang-Christensen et al. (Nature Med., July 2000, 6(7): 802-807, hereinafter "Tang-Christensen") and in view of Drucker et al. (US#5,789,379, hereinafter "Drucker"). The Examiner argues that the invention is obvious because Tang-Christensen teaches rats centrally administered with GLP-2 and Exendin(9-39), and Drucker teaches substitution of Gly<sub>2</sub>GLP-2 for GLP-2. Applicants respectfully assert that the rejection under 35 U.S.C. §103 is unwarranted because: i) there was no reasonable expectation of success; ii) the prior art references were improperly combined; and iii) the applicants proceeded contrary to the accepted wisdom in the art and obtained unexpected results.

#### **Lack of a reasonable expectation of success**

A reasonable expectation of success is required under any test of obviousness. MPEP §2143.02; see also *Amgen, Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 1207-08 (Fed. Cir. 1991). However, Tang-Christensen cannot be relied upon for a reasonable expectation of success. On page 803 of Tang-Christensen, the authors conclude that "prior administration of 10 µg Exendin (9-39) completely reversed the GLP-2 (1-33)(10 µg)-induced anorexia . . . returning food intake to the same level as animals receiving two consecutive injections of vehicle." Figure 3c provides data supporting this conclusion.

In summary, Tang-Christensen teaches two important concepts: 1) co-administration of GLP-2 and Exendin (9-39) has no effect compared to the control in appetite suppression; and 2) Exendin (9-39) does not enhance GLP-2 mediated anorexia, it reverses it. Thus, a person of ordinary skill in the art could not have a

reasonable expectation of success in combining GLP-2 or GLP-2 analogs (in view of Drucker) with Exendin (9-39) to enhance the anorectic effects of said GLP-2 or GLP-2 analog, because the prior art clearly taught that the opposite was true.

#### Improper combination of prior art references

Furthermore, Applicants assert that the obviousness rejection should be withdrawn because prior art references may not be combined if one of the references teaches away from their combination. *See e.g., In re Grasselli*, 713 F.2d 731, 743 (Fed. Cir. 1983); MPEP § 2145. In *Grasselli*, the court held that two references could not be combined to establish the interchangeability of antimony and alkali metal in a catalyst where one of the references expressly omitted antimony from the catalyst. Likewise, the references cited by the Examiner cannot be combined to establish the obviousness of the claimed enhancement of Gly<sub>2</sub>GLP-2's anorectic effects by Exendin (9-39) where one of the references (Tang-Christensen) specifically teaches that Exendin (9-39) reverses the anorectic effects of GLP-2. Furthermore, where Tang-Christensen teaches that GLP-2 and Exendin (9-39) combined have no appetite suppressing effects, the references cannot be combined to make obvious an invention that explicitly claims an anorectic effect.

#### Other Evidence of non-obviousness

Proceeding contrary to accepted wisdom in the art is evidence of nonobviousness. *In re Hedges*, 783 F.2d 1038, 228 USPQ 685 (Fed. Cir. 1986). Here, where the prior art teaches that GLP-2 and Exendin (9-39) combined do not affect appetite relative to vehicle controls, and where Exendin (9-39) reverses the anorectic effect of GLP-2, it is clear that Applicant's invention proceeds contrary to the accepted wisdom of the art.

Finally, evidence of unexpected results may be used to overcome a finding of obviousness. *In re Dillon*, 919 F.2d 688, 692-93 (Fed. Cir. 1990); MPEP § 2145. Tang-Christensen specifically teaches that Exendin (9-39) reverses the anorectic effects of

GLP-2. However, in paragraph [0058] of the specification Applicants report that "[r]emarkably, the inhibitory effects of icv hGly<sub>2</sub>GLP-2 on food intake in wild type mice were significantly more pronounced in the presence of co-administered exendin (9-39)." This statement is verified by figure 1c of the application disclosure. These data contradict the knowledge available to a person of ordinary skill in the art and represent an unexpected result over the prior art.

In sum, i) a prima facie case of obviousness was not established; ii) prior art references were improperly combined; and iii) Applicants proceeded contrary to the accepted wisdom in the art and obtained unexpected results. Thus, Applicants submit that a rejection of claims 1 and 6 as obvious under 35 U.S.C. §103(a) is improper.

## **CONCLUSION**

In sum, Applicants respectfully assert that claims 1, 6 and new claims 12 and 13 are allowable and request that a timely Notice of Allowance be issued in this case. If there are any remaining issues preventing allowance of the pending claims that may be clarified by telephone, the Examiner is requested to call the undersigned.

Respectfully submitted,

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